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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,058	06/21/2006	David Grahame Hardie	002.00270	2111

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,058	HARDIE ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14,16,19-29 and 31-35* is/are pending in the application.

4a) Of the above claim(s) *1,2,7-12,14,21-29 and 31-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6,16,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 January 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0807;0807;0807;0807;0807*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election, with traverse, of Invention II, Claims 3-5 and 16, in their response of April 10, 2008 is acknowledged. The elected invention is directed to a composition comprising LKB, STRAD, and MO25.

Applicants' traversal is based on the following arguments.

(A.) The Office's conclusion that Fryer et al, 2002 anticipates Claim 29 by teaching a method for identifying AMPK inhibitors is in error. Claim 29 recites the use of the compound of Claim 3, wherein said compound comprises MO25. There is no mention of recombinant MO25 in Fryer et al.

(B.) It is inappropriate to impose restriction between Group I(A)-(B) and Group II because said groups are related to one another and would require common areas of search.

(C.) The Restriction Requirement may oversimplify or otherwise mischaracterize the subject matter.

Theses arguments are, or are not, found to be persuasive for the following reasons.

(A) Reply: This argument is found to be persuasive.

(B) Reply: Lack of Unity cannot be overcome by a commonality between a sub-set of the claims.

(C) Reply: Applicants' argument is acknowledged.

The Restriction/Election requirement mailed March 13, 2008 is hereby replaced with the Restriction/Election below.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, Claims 1-5, 16, 19, and 20 drawn to a method for identifying a LKB1 modulator using a composition comprising STRAD and/or MO25 and said composition.

Group II, Claims 6-12, drawn to a cell capable of expressing LKB1, STRAD, and MO25.

Group III, Claim 14, drawn to a cellular method for making a composition comprising LKB1, STRAD, and MO25.

Group IV, Claims 21, 22, 31, 32, drawn to a kit comprising isolated LKB1, STRAD, and MO25.

Group V, Claims 23 and 24, drawn to a method for over-expressing LKB1.

Group VI, Claims 25 and 26, drawn to a method for identifying a MO25 binding partner.

Group VII, Claims 27 and 28, drawn to a method for identifying a MO25 genetic defect in PJS.

Group VIII, Claim 29, drawn to a method for identifying activators of AMPK.

Group IX, Claims 33 and 34, drawn to a peptide substrate for LKB1.

Group X, Claim 35, drawn to an antibody.

For each of Inventions I, IX, and X above, restriction to one of the following is also required. Therefore, election is required of one of Inventions I-X and, if Invention I, IX, or X is elected, one of Inventions (A)-(CC).

If Invention I is elected, elect one of:

(A.) An in vitro method

(B.) A cellular method

If Invention IX is elected, elect one of:

(C.) SEQ ID NO: 16

(D.) SEQ ID NO: 17

(E.) SEQ ID NO: 18

(F.) SEQ ID NO: 19

(G.) SEQ ID NO: 20

(H.) SEQ ID NO: 21

(I.) SEQ ID NO: 23

(J.) SEQ ID NO: 24

(K.) SEQ ID NO: 25

(L.) SEQ ID NO: 29

(M.) SEQ ID NO: 31

(N.) SEQ ID NO: 33

(O.) SEQ ID NO: 35

(P.) SEQ ID NO: 37

If Invention X is elected, elect one of:

(Q.) SEQ ID NO: 38

(R.) SEQ ID NO: 39

(S.) SEQ ID NO: 40

(T.) SEQ ID NO: 41

(U.) SEQ ID NO: 42

(V.) SEQ ID NO: 43

(W.) SEQ ID NO: 44

(X.) SEQ ID NO: 45

(Y.) SEQ ID NO: 46

(Z.) SEQ ID NO: 47

(AA.) SEQ ID NO: 48

(BB.) SEQ ID NO: 49

(CC.) SEQ ID NO: 50

The inventions listed as Group I relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they comprise the same or corresponding special technical feature, a composition comprising STRAD and/or MO25 and a method for identifying a LKB1 modulator using said composition. The products of Groups II and IV are not so linked to Group I as to be encompassed by said single general inventive concept because said products do not share a common structure and function with the product of Group I. The methods of Groups III and V-VIII are not linked so linked to Group I as to be encompassed by said single general inventive concept because said methods do not share the same modes of operation, functions, or effects of the methods of Group I. The methods of Groups I(A)-(B) do not use the same reagents or produce the same results. The methods of Groups IX(C)-(P) do not use the same reagents or produce the same results. The methods of Groups X(Q)-(CC) do not use the same reagents or produce the same results. In addition, the methods of Groups I, III, and V-VIII do not comprise all of the methods for making or using the products of Groups I, II, and IV.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention and sub-invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be

considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Peter Rogalskyj on May 14, 2008 a provisional election was made without traverse to prosecute Invention I, sub-invention A. The elected invention is directed to an in vitro, biochemical composition comprising LKB1, STRAD, and recombinant MO25 and a method for identifying a LKB1 modulator using said composition comprising. Affirmation of this election must be made by Applicant in replying to this Office action.

Claims 1-12, 14, 16, 19-29, and 31–35 are pending. Claims 1, 2, 7-12, 14, 21-29, and 31-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 3-6, 16, 19, and 20 are hereby examined.

Priority

The priority date granted for the instant invention is July 17, 2003, the filing date of UK 0316725.1, which disclosed the elected invention.

Information Disclosure Statement

Parts of the Information Disclosure Statements filed August 17, 2007 fails to comply with 37 CFR 1.98(a)(1), which requires the following:

Each foreign patent or published foreign patent application listed in an information disclosure statement must be identified by the country or patent office which issued the patent or published the application, an appropriate document number, and the publication date indicated on the patent or published application. (see MPEP 609 and 37 CFR 1.98 (3)(b)(4)).

Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication (see MPEP 609 and 37 CFR 1.98 (3)(b)(5)).

The information disclosure statement has been placed in the application file, but the improper references have not been considered. If Applicants wish for the references therein to be considered, a supplemental, corrected Information Disclosure Statement should be submitted. Any subsequent rejection, based on consideration of the supplemental Information Disclosure Statement, will not be considered new grounds for rejection.

Drawings-Objections

Figures 2, 10, 12, 19, 21, 25 26, and 30 are objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more

amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

The specification is objected to for containing hyperlinks. USPTO policy does not permit the USPTO, i.e, via an issued patent, to refer to any commercial sites, since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. Hyperlinks and other forms of browser-executable code, especially commercial site URLs, are not to be included in a patent application. (MPEP 608.01) The specification should be carefully checked and all URLs removed.

The drawings are objected to for having two Figures 4A.

The drawings are objected to for having two Figures 6A.

Specification-Objections

The specification is objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims

of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object e.g., "We claim" or "The claims are".

Applicants are reminded that every claim set must list all claims and the status thereof.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5, 16, 29, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claim 3, the phrase "A purified preparation comprising LKB1, STRAD, and recombinant MO25" renders the claim indefinite. It is unclear whether said phrase means a composition comprising only purified LKB1, purified STRAD, and purified recombinant MO25 or some other composition, such as a cellular lysate. The term "purified" is a relative term and neither the claims nor the specification define said term. The skilled artisan would not know the metes and bounds of the recited invention. Claims 4, 5, 16, 29, and 20, as dependent from Claim 3, are indefinite for the same reason. For purposes of examination, it is assumed that "A purified preparation comprising LKB1, STRAD, and recombinant MO25" means any non-cellular composition comprising LKB1, STRAD, and recombinant MO25.

For Claim 19, recitation of "identifying a compound for modulating cellular LKB1 activity…a preparation according to claim 3" renders the claim indefinite. As stated above, Claim 3 recites a non-cellular composition. Therefore, it is unclear whether Claim 19 is meant to recite "identifying a compound for modulating cellular LKB1 activity…a preparation according to claim 1" (claim 1 is a cellular method) or, alternatively, Claim 19 is meant to recite "identifying a compound for modulating LKB1 activity in vitro…a preparation according to claim 3" (Claim 3 is an in vitro, biochemical method). The skilled artisan would not know the metes and bounds of the recited invention. Claim 20, as dependent from Claim 19, is indefinite for the same reason. For purposes of examination, it is assumed that Claim 19 is meant to recite "identifying a compound for modulating LKB1 activity in vitro…a preparation according to claim 3".

Claims 19 and 20 are rendered indefinite for improper antecedent usage as follows.

For Claim 19, the phrase "a preparation according to Claim 3" should be corrected to "the preparation according to Claim 3".

For Claim 20, "the substrate" lacks antecedent basis.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 3-5, 16, 29, and 20 are rejected under 35 U.S.C. 112, first paragraph/ lack of enablement, because the specification does not reasonably provide enablement for an in vitro,

biochemical composition comprising any LKB1 protein, any STRAD protein, and any recombinant MO25 protein or methods of using said composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 3-6, 16, 19, and 20 are so broad as to encompass any in vitro, biochemical composition comprising any LKB1 protein, any STRAD protein, and any recombinant MO25 protein or methods of using said composition. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of compositions comprising an extremely large number of proteins broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired LKB1, STRAD, MO25 activities requires a knowledge of and guidance

with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the LKB1 protein disclosed by Boudeau et al, 2003 [0162].

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 3-6, 16, 19, and 20 which encompasses all in vitro, biochemical compositions comprising any LKB1 protein, any STRAD protein, and any recombinant MO25 protein or methods of using said compositions. The specification does not support the broad scope of Claims 3-6, 16, 19, and 20 because the specification does not establish: (A) the structural identity of any STRAD or MO25 protein contained within any in vitro, biochemical compositions used in the specification; (B) regions of the protein structure which may be modified without affecting the desired LKB1, STRAD, MO25 activities; (C) the general tolerance of the LKB1, STRAD, MO25 activities to modification of the proteins and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and

(E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of proteins is likely to have the desired LKB1, STRAD, MO25 activities.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any in vitro, biochemical composition comprising any LKB1 protein, any STRAD protein, and any recombinant MO25 protein or methods of using said compositions. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 3-6, 16, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of in vitro, biochemical compositions comprising any LKB1 protein, any STRAD protein, and any recombinant MO25 protein or methods of using said compositions. The specification teaches no such compositions because the specification fails to disclose the exact structural identity of any STRAD or MO25 protein contained within any in vitro, biochemical compositions used in the specification. Moreover, the specification fails to describe any representative species of

compositions by any identifying characteristics or properties other than the functionality of comprising proteins having LKB1, STRAD, and MO25 activities. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Allowable Subject Matter

No claims are allowable

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652